

21st Century Cures: Patients & the Patient Perspective
Statement of the Alpha-1 Foundation and COPD Foundation
Presented by Dr. Samantha Lindsay

Tuesday, August 19th, at 1:30 pm
The Bethany Center
18150 Bethany Center Drive
Lutz, FL 33558

Congressman Bilirakis thank you for convening this roundtable on the 21st Century Cures Initiative and for inviting the Alpha-1 Foundation and COPD Foundation; both of whom I am representing here today.

I am Dr. Samantha Lindsay and I have Alpha-1 Antitrypsin Deficiency, those of us with this genetic condition we simply call it Alpha-1. Alpha-1 may result in serious lung disease in adults and/or liver disease at any age. Alpha-1 is the leading identified genetic risk factor for developing chronic obstructive pulmonary disease (COPD). Alpha-1 (which is a rare disease) has cleverly associated itself with COPD a common disease that is currently the third leading cause of death. This pairing is an attempt to bring additional attention to Alpha-1 and to promote diagnosis at an earlier stage in the disease.

While I was attending medical training, at high altitude I began noticing difficulty with my breathing. I was only 41 years old and struggling to catch my breath! Unfortunately, Alpha-1 like most rare diseases has an average 7-year period from the onset of symptoms and visits with 5 different doctors prior to receiving an accurate diagnosis. I was diagnosed with COPD and not tested for Alpha-1 until 8 years later! The difference between COPD and Alpha-1 is that Alpha-1 is a genetic disorder where individuals like me are missing a protein. That protein when purified from the plasma of thousands of donations is administered intravenously and can stabilize the lung disease. To maintain a somewhat normal life, I must sleep and exercise with oxygen, and protect my lungs from environmental and biological factors that destroy elasticity of my lung tissue with the weekly use of intravenous augmentation therapy.

Alpha-1 end stage treatment is transplantation with all the attenuating problems. Alpha-1 can also affect children and their livers some of whom will need transplants to survive. I could tell you countless stories of people who are barely surviving day to day because they can't afford medication, can't get to doctors who know enough about the condition and struggle everyday because they can't do what they could before. For me, this means I may not be able to practice medicine as long as I would like or I may need a lung transplant sooner if my lungs start to deteriorate at a faster rate. It also limits how and where I practice medicine so that I limit my exposure to any type of infection that would negatively affect my lungs, which means I avoid hospitals. I must accommodate changes into my life that allow me to continue to work and not go onto disability.

If I had been diagnosed sooner my lungs would not be as bad and this is a common story. This disease poses significant burdens on patients and their families. It is also a financial encumbrance for those on augmentation therapy who must pay \$100 thousand to \$150 thousand dollars annually. As a physician, I

am proactive in testing for this condition and am encouraging other physicians to do the same. Even though I look healthy on the outside, my lungs are that of a 104 yr. old person.

Finding a cure is the Alpha-1 Foundation's top priority but our community has also taken responsibility for expediting drug development by investing in the establishment of a research infrastructure. Many orphan diseases have no therapy – but for those like me who do – we hope for the next generation of therapies. It would be an improvement in efficacy, quality of life, and cost if the second generation of drugs like aerosols, could be expedited for use in Alpha-1. However, the FDA has not been flexible and often holds companies to unattainable criteria when developing next generation drugs.

What is the solution? The Foundation endorses ideas that have come before the Committee during this process that calls for the FDA to be flexible in all of the areas where it currently has statutory authority. For Alpha-1 and COPD this includes the establishment of biomarkers. Much discussion has taken place over the past several years regarding the promise of biomarkers. The FDA established a pathway to approve biomarkers by issuing guidance. What is standing in the way of progress in this important area of therapeutic development? The COPD Foundation established a unique partnership amongst five pharmaceutical companies to capture pre-competitive industry data leading to their biomarker application. All of the pertinent NIH studies were used to populate the data set. This is a clear example of a patient organization that has been able to stimulate the participation of all stakeholders in a pre-competitive environment that will ultimately improve patient care and accelerate therapeutic development. It is imperative that we get approval for better drugs to treat these conditions and I am appealing to you to improve the FDA's review of Biomarkers and their qualification. Our lives depend on it.

The Alpha-1 Foundation endorses statements made by the National Organization for Rare Disorders (NORD) before the Committee on Energy and Commerce, Subcommittee on Health during various hearings on the 21st Century Cures initiative. NORD proposed that FDA should use its current authority and increase the use and visibility of the Accelerated Approval process by considering it for each new drug application. NORD noted that FDA would not need to establish any new programs or policies. Further, NORD underscored the importance of the patient voice before the Subcommittee when Dr. Marshall Summar said "When we ask patients 'What is the worst thing about your disease?', we are often surprised by their answers". The direct experiences of patients and their families are unique and extremely important to the process of drug discovery and development.

We have included a list of recommendations for rare disease drug development and more information about our organizations and these diseases in our written statement for your review.

Congressman, I understand that your father was a friend of the Alpha community and I hope that we can continue that friendship into the future and help find a cure for Alpha-1.

Recommendations for Rare Disease Drug Development Solutions

- Empower a HHS Rare Diseases Working Group that includes NIH, NCATS and FDA to propose a "Rare Disease Healthcare Improvement Plan."
- Alpha-1 drug discovery has 5-6 new medications in development that might be able to address the liver disease unique to Alpha-1. The therapies are not well capitalized and will likely die in the "Valley of Death" for lack of money. Much money can be saved by improving the regulatory cycle for new drugs.
- Small companies developing orphan drugs need an FDA process that facilitates instead of stifles clinical trials. Since people are dying from these rare diseases, a focus on efficacy more than safety would receive overwhelming support from our Rare Disease Community. We have new informatic tools that can follow drug safety in post marketing registries for the safety that is necessary for long term regulatory approval.
- Our country needs a robust program to establish biomarkers that can be used to expedite drug development for all entrants into a drug class. Clinical variables can be studied by Registries after drug approvals. The examples in Alpha-1 include CT densitometry and markers of liver fibrosis that are known but not well accepted as sufficient for drug approvals.
- Legislation is needed to force IRBs to host federated projects in which one IRB becomes primary for every clinical trial. Safety is improved by data sharing to all sites with real time analysis of adverse events.
- The Orphan Drugs Act has brought new drugs to rare disease but often stifles innovation for new products to enter the market, The Humanitarian Device Exemption (HDE) process works well by not having to prove efficacy for a rare disease before approval. Instead a Registry is necessary to define efficacy and extended safety after device approval. A similar process should be established for drugs. Both of these pathways are still slow to execute.
- Payment reform for rare disease medications has hit a crisis. The nurses and doctors that staff Alpha-1 clinics work harder than ever to appeal arbitrary coverage decisions for the rare diseases made by insurers. If drug approvals are obtained, high cost-sharing structures make some of these products inaccessible to the patients who need them the most, this is generally known as specialty tiering. The idea of an Orphan Protected Class within Medicare Part B and D would protect some of the rare disease drug access issues.
- PCORnet: The National Patient-Centered Clinical Research Network must be protected. These large scale registries known as Patient Powered Research Networks (PPRNs) and Clinical Data Research Networks (CDRNs) should be further empowered to assist with rare diseases. We are concerned about their future due to the politics surrounding the Affordable Care Act. This initiative will help with comparative effectiveness research for common diseases and is a mechanism to observe the natural history of rare diseases.

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More About Alpha-1

- Alpha-1 has been identified in nearly all populations and ethnic groups. It is estimated that about 1 in every 2,500 Americans have Alpha-1.
- People with Alpha-1 may remain healthy throughout their lives. Early diagnosis and avoiding risk factors, such as cigarette smoking, can help prevent Alpha-1 from causing disease.
- An estimated 19 million people in the United States have one normal and one defective alpha-1 gene. People with one normal gene and one defective gene (for example MZ) are called “carriers”. Carriers may pass the defective gene on to their children.
- Alpha-1 can lead to lung destruction and is often first diagnosed as asthma or smoking-related Chronic Obstructive Pulmonary Disease (COPD).
- Alpha-1 cannot be diagnosed by symptoms or by a medical examination alone; you need to get a simple, reliable blood test to know for sure.
- Alpha-1 is the most common known genetic risk factor for emphysema.
- Up to 3% of all people diagnosed with COPD may have undetected Alpha-1.
- Alpha-1 can also lead to liver disease. The most serious liver diseases are cirrhosis and liver cancer.
- The World Health Organization (WHO), American Thoracic Society (ATS), and the European Respiratory Society (ERS) recommend that everyone with COPD be tested for Alpha-1.

About The COPD Foundation

The COPD Foundation is a 501(c)(3) not-for-profit organization created in 2004, with offices in Washington, D.C. and Miami, FL. The COPD Foundation was established to undertake initiatives that result in expanded services for COPD and improve the lives of individuals affected by COPD. The Foundation’s activities focus on achieving these results through research, education and advocacy programs that will lead to prevention, and someday, a cure for this disease. Currently, there are 18 members in the Board of Directors who volunteer their time and resources to helping advance the

Mission

The COPD Foundation's mission is to prevent and cure Chronic Obstructive Pulmonary Disease and to improve the lives of all people affected by COPD.

Purpose

Chronic Obstructive Pulmonary Disease is a preventable and treatable disease. The COPD Foundation has been established to speed innovations which will make treatments more effective and affordable, undertake initiatives that result in expanded services for COPD patients, and improve the lives of patients with COPD and related disorders through research and education that will lead to prevention and someday a cure for this disease.

What is the Alpha-1 Foundation?

Mission Statement

The Alpha-1 Foundation is committed to finding a cure for Alpha-1 Antitrypsin Deficiency and to improving the lives of people affected by Alpha-1 worldwide. The Alpha-1 Foundation is a not-for-profit Florida corporation founded in 1995. A majority of the Board of Directors is either diagnosed with Alpha-1 or has a family member diagnosed with Alpha-1. The Foundation has developed a solid infrastructure to promote research and the development of new therapies for improving the quality of life for those diagnosed with Alpha-1. It has fostered collaborations with investigators throughout the United States and Europe, working closely with the National Institutes of Health (NIH), the Food and Drug Administration (FDA), individuals affected by Alpha-1, and the pharmaceutical industry to expedite the development of improved therapies. The Foundation participates in industry and government liaison groups and develops strategic alliances with government, industry and other national and international health and research organizations.

The most common signs and symptoms of Alpha-1

Symptoms related to the lung:

- Shortness of breath
- Wheezing
- Chronic bronchitis, which is cough and sputum (phlegm) production that lasts for a long time
- Recurring chest colds
- Less exercise tolerance
- Asthma that can't be completely reversed with aggressive medical treatment
- Year-round allergies
- Bronchiectasis

Symptoms related to the liver:

- Unexplained liver disease or elevated liver enzymes
- Eyes and skin turning yellow (jaundice)
- Swelling of the abdomen (ascites) or legs
- Vomiting blood (from enlarged veins in the esophagus or stomach)